31. (New) A process according to claim 1, wherein said reaction is stopped when the degree of hydrolysis is within the range of from 19.5-20.5%.

32 (New) A whey protein hydrolysate as prepared according to claim 12 or 13.

REMARKS

Claims 1, 6, 8, and 10-14 are amended, and claims 16-32 are added. Claims 1-3 and 4-32 are now pending. The amendments to the claims are not intended to surrender trivial or insubstantial variations in the amended claim elements that are not within the scope of the prior art.

The amendments to claim 1 are supported, for example, by the specification at page 5, lines 30-32 and by the specification at page 14, lines 12-15.

The amendments to claim 6 are supported, for example, by the specification at page 14, lines 12-15.

The amendments to claim 8 are supported, for example, by originally-filed claim 1.

The amendments to claim 10 are supported, for example, by the specification at page 5, lines 30-32.

The amendments to claim 11 are supported, for example, by the specification at page 8, lines 27-30.

The amendments to claim 12 are supported, for example, by the specification at page 5, lines 30-32 and the specification at page 8, lines 27-30.

The amendments to claim 13 are supported, for example, by the specification at page 5, lines 30-32.

The amendments to claim 14 are supported, for example, by the specification at page 9, lines 25-28.

New claim 16 is supported, for example, by the specification at page 4, lines 22-25.

New claims 17 and 18 are supported, for example, by the specification at page 15, lines 27-30.

New claim 19 is supported, for example, by the specification at page 5, lines 30-32.

New claim 20 is supported, for example, by the specification at page 5, lines 24-26.

New claim 21 is supported, for example, by the specification at page 5, lines 24-26.

New claim 22 is supported, for example, by the specification at page 5, lines 24-26.

New claim 23 is supported, for example, by the specification at page 5, line 12.

New claim 24 is supported, for example, by the specification at page 5, lines 9-17.

New claim 25 is supported, for example, for example, by originally-filed claim 1.

New claim 26 is supported, for example, by the specification at page 11, Table 1.

New claim 27 is supported, for example, by the specification at page 12, lines 18-21.

New claim 28 is supported, for example, by the specification at page 9, lines 1-2.

New claim 29 is supported, for example, by the specification at page 4, lines 18-20.

New claims 30 and 31 are supported, for example, by the specification at page 8, lines 27-30.

New claim 32 is supported, for example, by page 3, lines 23-24.

I. The 35 U.S.C. § 112 First Paragraph Rejections of the Claims

The Examiner rejected claims 8 and 11-13 under 35 U.S.C. § 112, first paragraph, alleging that those claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claims 8 and11-13 have been amended, thereby rendering this rejection moot.

II. The 35 U.S.C. § 112 Second Paragraph Rejections of the Claims

The Examiner rejected claims 1-12 under 35 U.S.C. § 112, second paragraph, alleging that those claims were indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Claims 1 and 12 have been amended, thereby rendering this rejection moot.

II. The 35 U.S.C. § 103(a) Rejection of the Claims

The Examiner rejected claims 1-3 and 5-15 under 35 U.S.C. § 103(a), alleging that those claims are unpatentable over JP 4-82898 in view of Lewis, Sr. (Hawley's Condensed Chemical Dictionary, 13th Edition, p. 937, (1997)). As this rejection may be maintained with respect to the

pending claims, it is respectfully traversed.

Independent claim 1 recites a process for preparing an angiotensin-converting enzyme (ACE)-inhibiting composition comprising preparing an aqueous solution of a whey protein fraction and a proteolytic enzyme, wherein the proteolytic enzyme is trypsin; holding said solution under conditions effective for reaction to partially hydrolyze said whey protein fraction to provide a hydrolysate having increased ACE-inhibiting activity; stopping the reaction; and drying said hydrolysate.

Independent claim 12 recites a process for preparing an angiotensin-converting enzyme (ACE)-inhibiting composition comprising: preparing an aqueous solution of a whey protein fraction produced by ion exchange and a proteolytic enzyme, wherein the proteolytic enzyme is trypsin; holding said solution under conditions effective for reaction to partially hydrolyze said whey protein fraction to provide a hydrolysate having increased ACE-inhibiting activity; stopping the reaction when a degree of hydrolysis is reached within the range of from 5.5 to 6.5%, wherein said hydrolysate is characterized by the following Molecular Weight Profile (HPLC)

Range (Daltons)	Soluble Peptides
> 5000	50 - 55%
2000 - 5000	15 - 20%
< 2000	30 - 35%; and

drying said hydrolysate.

Independent claim 13 recites a process for preparing an angiotensin-converting enzyme (ACE)-inhibiting composition comprising: preparing an aqueous solution of a whey protein fraction, prepared by ion exchange processing and characterized by a protein content of at least 94% and an ash content of less than 3%, and a proteolytic enzyme, wherein the proteolytic enzyme is trypsin; and holding said solution under conditions effective for reaction to partially hydrolyze said whey protein fraction to provide a hydrolysate having increased ACE-inhibiting activity.

To establish a *prima facie* case of obviousness, the Examiner has the burden to establish three basic elements. First, the Examiner must establish that there is some suggestion or motivation, either in the cited references themselves or in the knowledge generally available to an art worker, to modify the reference or to combine reference teachings so as to arrive at the claimed invention.

Second, the Examiner must establish that there is a reasonable expectation of success. Finally, the Examiner must establish that the prior art reference teaches or suggests all the claim limitations. M.P.E.P. § 2143.

Applicant respectfully asserts that the Examiner has failed to establish that either the cited documents or the knowledge generally available to an art worker at the time the application was filed provides a suggestion or motivation to combine or modify the cited documents so as to arrive at Applicant's claimed invention. The teaching or suggestion to arrive at the claimed invention must be found in the prior art, not in Applicant's disclosure. M.P.E.P. § 2143 citing with favor, *In re Vaeck*, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991); emphasis added. The Examiner must provide specific, objective evidence of record for a finding of a suggestion or motivation to combine the reference teachings and must explain the reasoning by which the evidence is deemed to support such a finding. *In re Sang Su Lee*, 277 F.3d 1338, 61 U.S.P.Q.2D 1430 (Fed. Cir. 2002); emphasis added. Mere conclusory statements do not fulfill the Examiner's burden. *Id.*; underline added As has been stated (*Id.* at 1433):

> [t]he factual inquiry whether to combine references must be thorough and searching. It must be based on objective evidence of record. This precedent has been reinforced in myriad decisions, and cannot be dispensed with. *See, e.g., Brown & Williamson Tobacco Corp. v. Philip Morris Inc.*, 229 F.3d 1120, 1124-25, 56 U.S.P.Q.2d 1456, 1459 (Fed. Cir. 2000) ("a showing of a suggestion, teaching, or motivation to combine the prior art references is an 'essential component of an obviousness holding'") (*quoting C.R. Bard, Inc., v. M3 Systems, Inc.*, 157 F.3d 1340, 1352, 48 U.S.P.Q.2d 1225, 1232 (Fed. Cir. 1998)); *In re Dembiczak*, 175 F.3d 994, 999, 50 U.S.P.Q.2d 1614, 1617 (Fed. Cir. 1999) ("Our case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references."); *In re Dance*, 160 F.3d 1339, 1343, 48 U.S.P.Q.2d 1635, 1637 (Fed. Cir. 1998) (there must be some motivation, suggestion, or teaching of the desirability of making the specific combination that was made by the applicant); *In re Fine*, 837 F.2d 1071, 1075, 5 U.S.P.Q.2d 1596, 1600 (Fed. Cir. 1988) ("'teachings of references can be combined only if there is some suggestion or incentive to do so.'") (emphasis in original) (*quoting ACS Hosp. Sys., Inc. v. Montefiore Hosp.*, 732 F.2d 1572, 1577, 221 U.S.P.Q. 929, 933 (Fed. Cir. 1984)).

A factor cutting against a finding of motivation to combine or modify the prior art is when the prior art teaches away from the claimed combination. A reference may be said to teach away

when a person of ordinary skill, upon reading the reference would be led in a direction divergent from the path the applicant took. *In re Gurley*, 27 F.3d 551, 31 U.S.P.Q. 2d 1130, 1131 (Fed. Cir. 1994); *United States v. Adams*, 383 U.S. 39, 52, 148 U.S.P.Q. 479, 484 (1966); *In re Sponnoble*, 405 F.2d 578, 587, 160 U.S.P.Q. 237, 244 (C.C.P.A. 1969); *In re Caldwell*, 319 F.2d 254, 256, 138 U.S.P.Q. 243, 245 (C.C.P.A. 1963).

As the Examiner acknowledges at page 3 of the final Office Action mailed July 02, 2002, JP 4-82898 does not teach or suggest the use of trypsin for use in the hydrolysis. In fact, JP 4-82898 teaches away from the combination of the documents. Trypsin is a serine peptidase (see pages 177-178 of Biochemical Pathways, edited by Gerhard Michal (1999), copy provided herewith). In contrast, JP 4-82898 directs the art worker to use an aspartic proteinase. Hawley simply presents generic definitions, for example, of a "protease", a "protein hydrolyzate" and "proteolysis". Hawley does not teach or suggest that the art worker should ignore JP 4-82898's teaching directing the art worker to use an aspartic proteinase. As Applicant has taught at page 2, lines 25-27 and at page 15, lines 20-25 of specification, the specificity of the enzyme used in the hydrolysis has a pronounced effect on the resulting ACE-inhibitory activity of the hydrolysates. Thus, the Examiner has failed to establish that either the cited documents or the knowledge generally available to an art worker at the time the application was filed provides a suggestion or motivation to combine or modify the cited documents so as to arrive at Applicant's claimed invention.

For the reasons described hereinabove, Applicant submits that the Examiner has not make out a *prima facie* case of obviousness because the Examiner has not established that the art provides a suggestion or motivation to combine the documents. Therefore, Applicant respectfully requests that this rejection of claims 1 and 12 under 35 U.S.C. § 103(a) be withdrawn.

What does this show? Trypsin and Pepsin are both used!

CONCLUSION

Applicant respectfully submits that the claims are in condition for allowance and notification to that effect is requested. The Examiner is invited to telephone Applicant's attorney (612-359-3265) to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,
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Date 12-31-02 By _____
Robert J. Harris, Ph.D.
Reg. No. 37,346

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Box RCE, Commissioner of Patents, Washington, D.C. 20231, on this 31st day of December, 2002.

Name Dawn M. Poole Signature Dawn M. Poole

Clean Version of the Pending Claims

1. (Twice Amended) A process for preparing an angiotensin-converting enzyme (ACE)-inhibiting composition comprising:

preparing an aqueous solution of a whey protein fraction and a proteolytic enzyme, wherein the proteolytic enzyme is trypsin;

holding said solution under conditions effective for reaction to partially hydrolyze said whey protein fraction to provide a hydrolysate having increased ACE-inhibiting activity;

stopping the reaction; and

drying said hydrolysate.

2. A process according to claim 1 wherein the proteolytic enzyme is inactivated.

3. A process according to claim 1 wherein the proteolytic enzyme is inactivated by heating following hydrolysis.

5. A whey protein hydrolysate as prepared according to claim 1.

6. (Twice Amended) A treatment regimen for a mammal to inhibit angiotensin-converting enzyme (ACE), said regimen comprising:

orally administering to the mammal, a product prepared according to claim 1, 12, or 13 in amounts and at intervals effective to inhibit ACE activity.

7. A process according to claim 1, wherein said hydrolysate is characterized by the following Molecular Weight Profile (HPLC)

Range (Daltons)	Soluble Peptides
> 5000	50 - 55%
2000 - 5000	15 - 20%
< 2000	30 - 35%.

8. (Once Amended) A process according to claim 1, wherein said whey protein fraction is a whey protein isolate.

9. A process according to claim 1, wherein said reaction is stopped when the degree of hydrolysis is within the range of from 5.5 to 6.5%.

10. (Once Amended) A process according to claim 1, wherein said whey protein fraction is produced by ion exchange and characterized by a protein content of at least 94% and an ash content of less than 3%.

11. (Once Amended) A process according to claim 10, wherein said reaction is stopped when the degree of hydrolysis is within the range of from 5.5 to 6.5%.

12. (Once Amended) A process for preparing an angiotensin-converting enzyme (ACE)-inhibiting composition comprising:

preparing an aqueous solution of a whey protein fraction produced by ion exchange and a proteolytic enzyme, wherein the proteolytic enzyme is trypsin;

holding said solution under conditions effective for reaction to partially hydrolyze said whey protein fraction to provide a hydrolysate having increased ACE-inhibiting activity;

stopping the reaction when a degree of hydrolysis is reached within the range of from 5.5 to 6.5%, wherein said hydrolysate is characterized by the following Molecular Weight Profile (HPLC)

Range (Daltons)	Soluble Peptides
> 5000	50 - 55%
2000 - 5000	15 - 20%
< 2000	30 - 35%; and

drying said hydrolysate.

13. (Once Amended) A process for preparing an angiotensin-converting enzyme (ACE)-inhibiting composition comprising:

preparing an aqueous solution of a whey protein fraction, prepared by ion exchange processing and characterized by a protein content of at least 94% and an ash content of less than 3%, and a proteolytic enzyme, wherein the proteolytic enzyme is trypsin; and

holding said solution under conditions effective for reaction to partially hydrolyze said whey protein fraction to provide a hydrolysate having increased ACE-inhibiting activity.

14. (Once Amended) A process according to claim 13, wherein said hydrolysate is characterized by the following Molecular Weight Profile (HPLC)

Range (Daltons)	Soluble Peptides
> 5000	50 - 55%
2000 - 5000	15 - 20%
< 2000	30 - 35%.

15. A process according to claim 14, wherein said reaction is stopped when the degree of hydrolysis is within the range of from 5.5 to 6.5%.

16. (New) A process according to claim 1 or 12, wherein the whey protein fraction has an ash content of <3%.

17. (New) A process according to claim 1, 12, or 13, wherein the whey protein fraction has a mineral content of calcium of 15-20 meq/kg.

18. (New) A process according to claim 1, 12, or 13, wherein the whey protein fraction has a mineral content of magnesium of <1 meq/kg.

19. (New) A process according to claim 1 or 12, wherein the whey protein fraction has a protein content of at least 35%.

20. (New) A process according to claim 1 or 12, wherein the whey protein fraction has a protein content that varies by 0 to 25% from 97.5 ± 1.0%.

21. (New) A process according to claim 1 or 12, wherein the whey protein fraction has a protein content that varies by 5 to 10% from 97.5 ± 1.0%.

22. (New) A process according to claim 1, 12, or 13, wherein the whey protein fraction has a protein content that varies less than 5% from 97.5. ± 1.0%.

23. (New) A process according to claim 1, 12, or 13, wherein the whey protein fraction has a protein content of 97.5. ± 1.0%.

24. (New) A process according to claim 1, 12, or 13, wherein the whey protein fraction is characterized as follows:

Analysis	Specification	Typical Range
Moisture (%)	5.0 max	4.7 ± 0.2
Protein, dry basis (N x 6.38)(%)	95.0 min.	97.5 ± 1.0
Fat (%)	1.0 max	0.6 ± 0.2
Ash (%)	3.0 max	1.7 ± 0.3
Lactose (%)	1.0 max	<0.5
pH	6.7 - 7.5	7.0 ± 0.2.

25. (New) A process according to claim 12 or 13, wherein the whey protein fraction is a whey protein isolate.

26. (New) A process according to claim 1, 12, or 13, wherein the proteolytic enzyme is porcine trypsin.

27. (New) A process according to claim 1, 12, or 13, further comprising concentrating said hydrolysate.

28. (New) A process according to claim 1 or 12, wherein the hydrolysate is spray-dried.

29. (New) A process according to claim 1, wherein the whey protein fraction is prepared by ion-exchange processing.

30. (New) A process according to claim 1, wherein said reaction is stopped when the degree of hydrolysis is within the range of from 11.0-12.5%.

31. (New) A process according to claim 1, wherein said reaction is stopped when the degree of hydrolysis is within the range of from ~~19.5-20.5%~~.

32. (New) A whey protein hydrolysate as prepared according to claim 12 or 13.